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ORIGINAL RESEARCH

Glucagon-Like Peptide-1 Receptor Agonists vs Dipeptidyl Peptidase-4 Inhibitor Use on Risk of Asthma Exacerbation Among Diabetic Patients with Co-Morbid Asthma in Hong Kong

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Background: Co-existing asthma and diabetes mellitus (DM) are common, and there has been a debate on whether glucagon-like peptide-1 (GLP-1)-based therapies, such as GLP-1 receptor agonists (GLP-1RA) and inhibitors of dipeptidyl peptidase-4 (DPP-4i), confer benefits in these patients due to their anti-inflammatory effects in chronic inflammatory diseases.

Methods: A territory-wide retrospective cohort study was conducted in Hong Kong among adult patients with co-existing asthma and DM to examine the impact of add-on GLP-1RA or DPP-4i on asthma exacerbations, ranging from mild exacerbations managed in outpatient settings to severe exacerbations requiring hospitalization. Adult patients were prescribed DPP-4i or GLP-1RA in year 2018 and for at least 6 months in Hospital Authority of Hong Kong were included. These patients were followed till 31st December 31, 2023. Propensity score matching was performed using optimal full matching, which is a sub-classification-based approach in which treated and control subjects are assigned to matched subclasses.

Results: A total of 3295 patients with both asthma and DM, 3193 treated with DPP-4i and 102 treated with GLP-1RA, were included in the study. There were 1191 (36.1%) male patients with a mean age of 68.0 ± 14.2 years. There were 2531 (76.8%) patients with moderate-to-severe asthma according to Global Initiative for Asthma (GINA) Steps 3 to 5. GLP-1RA-treated patients had significantly lower risks of hospitalized asthma exacerbation (Average Treatment Effect on the Treated (ATT) Mean Ratio of 0.513, $p < 0.001$), ad hoc outpatient visits with OCS (ATT Mean Ratio of 0.343, $p = 0.005$), emergency visits (ATT Mean Ratio of 0.378, $p = 0.009$), and all asthma exacerbations (ATT Mean Ratio of 0.419, $p < 0.001$) compared with the DPP-4i group.

Conclusion: GLP-1RA, compared with DPP-4i, as an add-on treatment for patients with co-existing DM and asthma was associated with a lower risk of asthma exacerbation. The use of GLP-1RA among diabetic patients with comorbid asthma may be considered though validation in clinical trials is needed.

Keywords: acute exacerbation, asthma, GLP-1 receptor antagonist, DPP-4 inhibitor

Introduction

Asthma and diabetes mellitus (DM) are both common chronic medical diseases. For diabetes, it is a common among adults in Hong Kong, with prevalence of about 10%.[1] Asthma is also another common medical condition in Hong Kong with more than 330000 patients suffering from asthma.[2] For asthma, environmental factors such as air pollution has been well recognized to be an important trigger.[3] Chronic airway inflammation was also a hallmark feature in asthma, involving various pro-inflammatory cytokines.[4] The co-existence of asthma and DM was also reported with increasing prevalence.[5] The co-existence of asthma and DM was also reported to be linked to worse asthma control.

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Glucagon-like peptide-1 (GLP-1)-based therapies, such as GLP-1 receptor agonists (GLP-1RA)[6,7] and inhibitors of dipeptidyl peptidase-4 (DPP-4i)[8–10] which are GLP-1 inactivating enzymes, have been developed for the treatment of diabetes mellitus. GLP-1-based therapies are useful in diabetic control. GLP-1RA also can promote weight loss and reduce cardiovascular disease outcomes in patients with existing atherosclerotic cardiovascular disease. There are also data suggesting that GLP-1-based therapies also demonstrate anti-inflammatory effects in chronic inflammatory diseases, including asthma.[11] The common adverse effects of GLP-1RA include nausea, vomiting, and diarrhea. GLP-1 has demonstrated anti-inflammatory effects on pancreatic islets and adipose tissue, contributing to lowering glucose levels in DM.[12,13] The anti-inflammatory effects were also observed in other organs such as the lungs.[11,14] GLP-1 receptor was also found to be found expressed abundantly in human lung, especially in vascular and smooth muscle tissues.[15,16] The GLP-1 receptor was also shown to be expressed in human eosinophils and neutrophils.[17] Studies suggested the possible role of GLP-1 receptor in asthma include smooth muscle relaxation and structural medication.[16] GLP-1 was also proposed to exert regulatory functions in innate immune cells, especially macrophages.[18] As GLP-based therapy, DPP-4i also raise endogenous GLP-1 but its pulmonary effects are weaker.[19]

Based on the knowledge of the anti-inflammatory effects of GLP-1-based therapies, these agents have been assessed for use among patients with respiratory diseases such as asthma.[20–22] Both DPP-4i and GLP-1RA were studied in asthma patients. The use of DPP-4i has been shown to reduce the risk of asthma and also asthma exacerbations.[23]

For GLP-1RA, a study demonstrated a beneficial effect on reducing asthma exacerbation relative to sulfonylureas, particularly among asthma patients with two or more emergency department visits.[24] In a retrospective study, patients starting on GLP-1RA were also reported to have fewer asthma exacerbations and improved asthma symptoms than those initiating the alternative agents (SGLT-2 inhibitors, DPP-4i, sulfonylurea, and basal insulin) within 6 months of drug initiation.[25] A meta-analysis also suggested a modest reduction in the incidence of asthma in patients with type 2 diabetes or obesity using GLP-1 receptor-based agonist treatments.[26]

However, the observed benefits of DPP-4i and GLP-1RA have also been challenged by other studies. One study suggested that there were no differences in asthma control between patients treated with or without DPP-4i.[27] The use of DPP-4i and GLP-1RA was also suggested to be associated with poorer asthma control than metformin.[28] The results from the above recently published studies indicate that controversies remain regarding GLP-1-based therapies among patients with asthma. Also, there is a lack of dedicated study that directly compares DPP-4i and GLP-1RA in diabetic patients with co-morbid asthma, whether there is a difference in asthma exacerbation rate among patients prescribed with DPP-4i or GLP-1RA. To further complicate this situation, there has been a lack of data on the beneficial effects of DPP-4i and GLP-1RA on asthma control, in particular real-world Asian data with long term follow up. As such, we propose the current study to compare the efficacy of DPP-4i versus GLP-RA in preventing asthma exacerbations among DM patients with co-morbid asthma in Hong Kong.

Materials and Methods

This is a territory-wide study conducted in Hong Kong to study the clinical efficacy of DPP-4i versus GLP-1RA in DM patients with asthma. Adult patients with DM and asthma, managed by the Hong Kong Hospital Authority (HKHA) in 2018, were included. They were prescribed DPP-4i or GLP-1RA for at least 6 months within the study period. These patients were followed from 1st January 2018 (or the start date of DPP-4i or GLP-1RA, whichever is later) to 31st December, 2023 (or the date of discontinuation of DPP-4i or GLP-1RA or death, whichever is earlier) (Figure 1). This study utilized electronic health records from the Clinical Data Analysis and Reporting System (CDARS) managed by the HKHA. HKHA is a public healthcare service provider that manages 43 hospitals and institutions and 123 outpatient clinics, covering more than 90% of the Hong Kong population since 1993.[29] The CDARS captures medical information including diagnosis, drug prescription details, demographics, admissions, medical procedures, and laboratory results. The asthma diagnostic code in CDARS was validated with a positive predictive value (PPV) of 85.0% (95% confidence interval = 80.1–89.9%).[30]

The inclusion criteria were adult patients (age ≥ 18 years) with a diagnosis of asthma identified by the International Classification of Diseases, 9th Revision (ICD-9) code of 493 and DM with ICD-9 code of 250 in 2018. Patients with a co-existing ICD-9 code of 496, indicating a co-existing diagnosis of COPD, and patients who received both DPP-4is

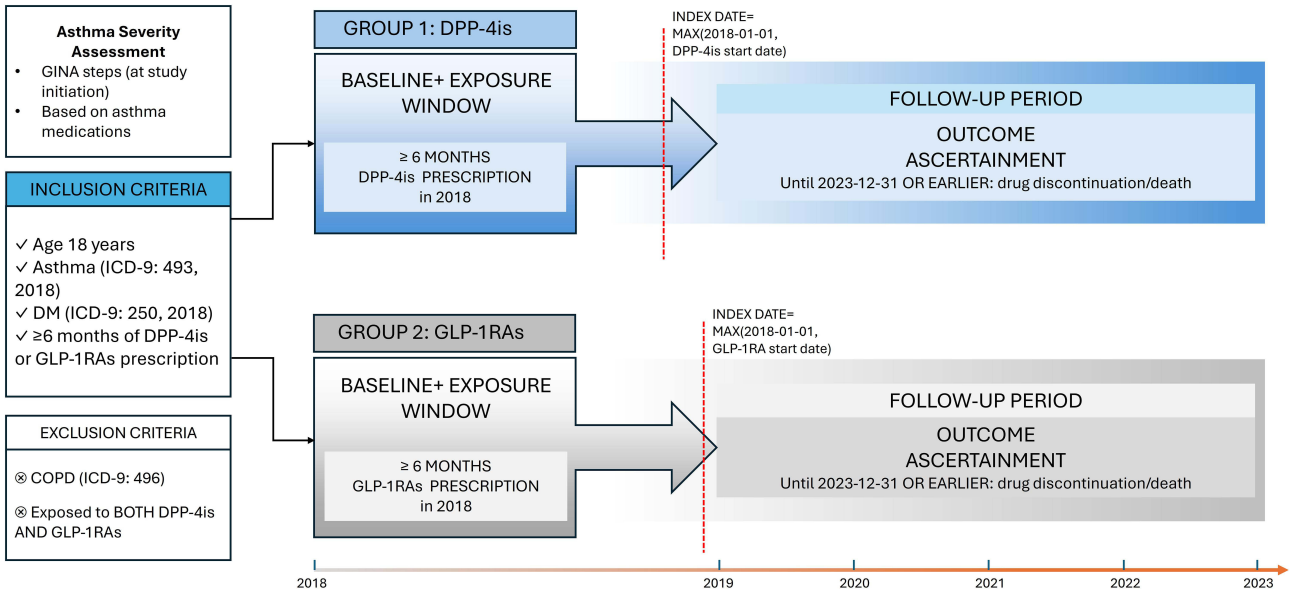

Figure 1 Study design.

and GLP-1RA during the inclusion period were excluded. Demographic (age and sex) and clinical characteristics (Charlson comorbidity index (CCI), presence of comorbidities and medications for asthma and DM, and baseline creatinine level) were retrieved from the CDARS. The medication the patients prescribed for asthma at the time of study initiation was used to define asthma severity as GINA steps. This study was approved by the Institutional Review Board of the University of Hong Kong and the Hospital Authority Hong Kong West Cluster (UW 23-510). Patient informed consent was waived as this was a retrospective study without active patient recruitment, and all retrieved clinical data were de-identified.

Asthma exacerbations of different severities, ranging from ad hoc outpatient visits with oral corticosteroid prescriptions to emergency department visits without hospitalization and hospitalization, were retrieved from the CDARS.

The primary outcome was the number of hospitalized asthma exacerbations. The secondary outcomes included the number of ad hoc outpatient visits with oral corticosteroid prescriptions (at least oral prednisolone 20 mg daily for 5 days), emergency department visits without hospitalization, and the number of asthma exacerbations of any severity.

Statistical Analysis

Categorical variables were expressed as the actual numbers (percentages). Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR). Between-group comparisons of continuous variables were performed using the independent *t*-test or Mann–Whitney *U*-test, and categorical variables were compared using the chi-square test or Fisher's exact test. Measures, including regular and conditional mean, SD, and IQRs (25th to 75th percentiles), were introduced to compare medical outcome event counts before and after matching. Here, conditional refers to calculations based on nonzero event counts. Causal effect estimation in observational studies requires comparison of medical outcomes between treated and control groups with similar covariate distributions to mitigate confounding bias.

Propensity score matching was performed using optimal full matching in R with the MatchIt package (version 4.7.2), which calls functions from the *optmatch* package for optimal full matching.[31–33] The covariates that were significantly different at baseline or clinically associated with asthma exacerbation risk were matched. Unlike fixed-ratio nearest-neighbor matching, optimal full matching is a subclassification-based approach in which treated and control subjects are assigned to matched subclasses, each containing at least one treated and one control subject. Full matching does not necessarily discard subjects; instead, it generates matching weights for all included individuals. Consequently, the nominal numbers of treated and control subjects can remain unchanged before and after matching, whereas post-

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matching covariate balance statistics can be computed using these weights. Accordingly, the adjusted means, absolute standardized differences, variance ratios, and Kolmogorov–Smirnov statistics reflect the weighted matched pseudo-population rather than the original unweighted sample. Weighted Kolmogorov–Smirnov statistics were computed based on the standard empirical distribution function approach and extended to incorporate matching weights.[34–36] The analysis estimated the average treatment effect in the treated (ATT) using a weighted regression model with marginal standardization, in which predicted outcomes under treatment and control were averaged over the treated population while incorporating the full-matching weights.[33,37] Standard errors were estimated using subclass-clustered variance estimation to account for the matched structure.[33,38] Thus, the analysis reflects the effect of treatment among treated individuals, with covariate balance improved through weighting rather than by reducing the cohort size. Therefore, the effective sample size, a precision-equivalent number of independent observations in the weighted sample, is more informative than the nominal sample size for interpreting the matched analysis.[36]

Statistical significance was determined at a level of $p = 0.05$.

Results

In 2018, there were 14379 patients with asthma (without COPD) and DM were followed up in the HKHA. Among these patients, there were 3193 treated with DPP-4i, 102 treated with GLP-1RA and 204 with both DPP-4i and GLP-1RA. Thus, only 3293 patients treated with DPP-4i or GLP-1RA were included in the final analysis. The patient selection flow diagram is shown in Figure 2. The baseline clinical characteristics of the patients are summarized in Table 1. The matching results are shown in Supplementary Figure 1.

There were 1191 (36.1%) male patients with a mean age of 72.1 ± 14.6 years. There were 2531 (76.8%) patients with moderate-to-severe asthma according to Global Initiative for Asthma (GINA) Steps 3 to 5. The matched cohorts were constructed through PSM on observed covariates including age, sex, GINA treatment steps, the presence of asthma exacerbation in the previous 12 months, CCI, phenotype as determined by blood eosinophil count (cutoff at 150 cells/μL), and the presence of underlying cardiovascular risk factors and diseases. After optimal full matching, the effective sample size was 421.65 in the DPP-4i group and 102 in the GLP-1RA group. This provided approximately four effective controls per treated patient, supporting adequate ATT analysis while reflecting the weighting required to achieve covariate balance. In addition, the absolute Standardized Mean Differences (SMDs) between the treated and control groups of all covariates were within 0.05, the adjusted variance ratios were close to 1.0, and the weighted Kolmogorov–Smirnov statistics were smaller than 0.1, indicating a good distributional balance.

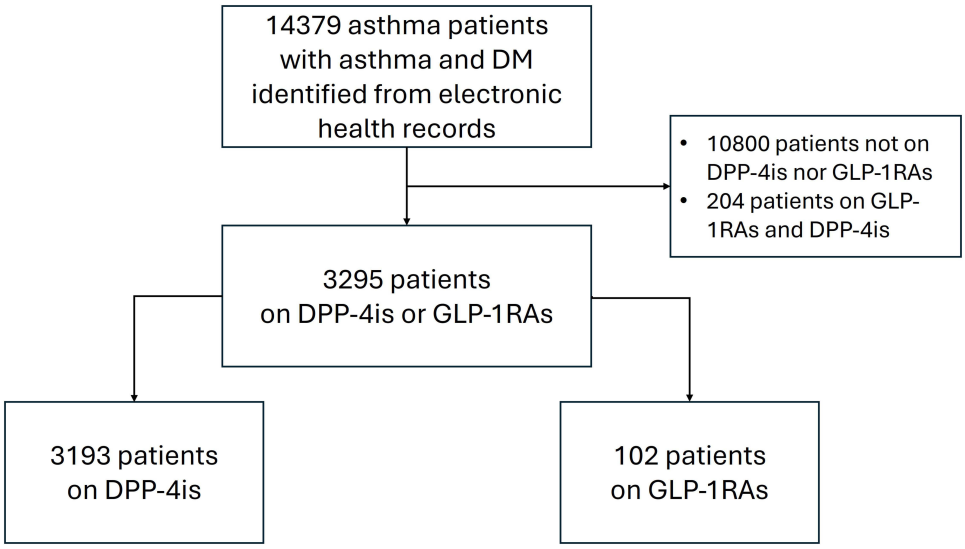

Figure 2 Patient selection flow diagram.

Table 1 Baseline Clinical Characteristics of the Included Patients

	Whole Cohort (n = 3295)	DDP-4i (n = 3193)	GLP-1RA (n = 102)	p-value Before Matching	SMDs		Variance Ratios		Weighed KS Statistic	
					Before Matching	After Matching	Before Matching	After Matching	Before Matching	After Matching
Age (mean (SD))	72.1 (14.6)	72.6 (14.3)	54.3 (12.9)	<0.001	−1.419	−0.026	0.807	0.962	0.526	0.06
Male (%)	1191 (36.1)	1143 (35.8)	48 (47.1)	0.020	0.113	0.014	–	–	0.113	0.014
Asthma severity by GINA Steps (%)				0.644	0.078	−0.012	19.256	1.011	0.057	0.034
1–2	764 (23.2)	735 (23.0)	29 (28.4)							
3	1260 (38.2)	1223 (38.3)	37 (36.3)							
4	428 (13.0)	418 (13.1)	10 (9.8)							
5	843 (25.6)	817 (25.6)	26 (25.5)							
Co-morbidities										
AF (%)	357 (10.8)	355 (11.1)	2 (2.0)	0.003	−0.092	0.003	–	–	0.092	0.003
Hyperlipidaemia (%)	1441 (43.7)	1404 (44.0)	37 (36.3)	0.123	−0.077	−0.008	–	–	0.077	0.008
Ischaemic heart disease (%)	419 (12.7%)	411 (12.9%)	8 (7.8%)	0.133	−0.050	−0.007	–	–	0.050	0.007
Heart failure (%)	308 (9.3%)	304 (9.5%)	4 (3.9%)	0.056	−0.056	0.001	–	–	0.056	0.001
CCI (Mean (SD))	4.47 (2.68)	4.52 (2.68)	2.77 (1.90)	<0.001	−0.919	−0.012	0.504	0.961	0.330	0.058
Any exacerbation in the preceding year (%)	171 (5.2%)	166 (5.2%)	5 (4.9%)	0.894	0.025	−0.042	2.039	1.256	0.010	0.020
Eosinophilic phenotype (%)	1582 (48.0%)	1527 (47.8%)	55 (53.9%)	0.225	0.061	−0.026	–	–	0.061	0.026

Abbreviations: DDP-4i, dipeptidyl peptidase-4 inhibitor; GLP-1RA, Glucagon-Like Peptide-1 Receptor Agonists; SMDs, Standardized Mean Differences; SD, Standard deviation; KS statistic, Kolmogorov–Smirnov statistic; GINA, Global Initiative for Asthma; AF, Atrial fibrillation; CCI, Charlson Comorbidity Index.

Table 2 Outcomes for Treatment and Control Groups

Outcomes	Mean Number of Events (Condition mean ± SD)		ATT Mean Ratio (SE)	p-value
	GLP-1RA Group (n = 102)	DPP-4i Group (n = 3193)		
Hospitalized asthma exacerbations	0.50 ± 3.02	0.83 ± 5.20	0.513 (0.087)	<0.001
Ad hoc outpatient visits with OCS	0.56 ± 1.68	0.81 ± 2.90	0.343 (0.231)	0.005
Emergency department visits	0.26 ± 1.03	0.29 ± 1.50	0.378 (0.238)	0.009
Asthma exacerbations of any severity	1.31 ± 4.78	1.95 ± 6.97	0.419 (0.165)	<0.001

Abbreviations: DDP-4i, Dipeptidyl peptidase-4 inhibitor; GLP-1RA, Glucagon-Like Peptide-1 Receptor Agonists; SE, Standard error; OCS, oral corticosteroids; SD, Standard deviation.

For count outcomes, weighted Poisson regression models with a log link were fitted in the propensity-score-matched cohort using the full-matching weights. Models included treatment group and prespecified covariates used for matching. Treatment effects were estimated as ATT mean ratios through g-computation using marginal standardization, calculated as the ratio of predicted mean outcomes under treatment and predicted mean outcomes under control among the treated population. Since overdispersion was observed, we also fitted quasi-Poisson model as a less sensitivity remedy, which retains the Poisson log-link mean structure while estimating a dispersion parameter. The quasi-Poisson yielded the same ATT mean ratios as the Poisson models and remained significant after using overdispersion-adjusted standard errors.

Hospitalized Asthma Exacerbations

Eleven patients (10.8%) in the GLP-1RA group and 516 (16.2%) in the DPP-4i group developed hospitalized asthma exacerbations. The conditional mean number of hospitalized asthma exacerbation was 0.50 ± 3.02 in GLP-1RA group and 0.83 ± 5.20 in DPP-4i group. The GLP-1RA (treatment) group was associated with a 48.7% lower expected number of events than the DPP-4i (control) group in the treated population (ATT mean ratio = 0.513 with a standard error (SE) of 0.087, $p < 0.001$) (Table 2).

Ad hoc Outpatient Visits with Oral Corticosteroid Prescriptions

Sixteen patients (15.8%) in the GLP-1RA group and 556 (17.4%) in the DPP-4i group had ad hoc outpatient visits with oral corticosteroid prescriptions. The conditional mean number of ad hoc outpatient visits with oral corticosteroid prescriptions episodes were 0.56 ± 1.68 in the GLP-1RA group and 0.81 ± 2.90 in the DPP-4i group. The GLP-1RA (treatment) group had a 65.7% lower expected number of events than the DPP-4i (control) group in the treated population (ATT Mean Ratio of 0.343, SE = 0.231, $p = 0.005$) (Table 2).

Emergency Department Visits Without Hospitalization

Eleven patients (10.8%) in the GLP-1RA group and 252 (7.9%) in the DPP-4i group had emergency department visits without hospitalization. The mean number of emergency department visits without hospitalization episodes were 0.26 ± 1.03 in the GLP-1RA group and 0.29 ± 1.50 in the DPP-4i group. The GLP-1RA (treatment) group was associated with a 62.2% lower expected number of events than the DPP-4i (control) group in the treated population (ATT Mean Ratio 0.378, SE = 0.238, $p = 0.009$) (Table 2).

Asthma Exacerbations of Any Severity

There were 27 patients (26.7%) in the GLP-1RA group and 875 (27.4%) in the DPP-4i group developed asthma exacerbations. The mean number of any asthma exacerbation episodes were 1.31 ± 4.78 in the GLP-1RA group and 1.95 ± 6.97 in the DPP-4i group. The GLP-1RA (treatment) group was associated with a 58.1% lower expected number of events than the DPP-4i (control) group in the treated population (ATT Mean Ratio = 0.419, SE = 0.165, $p < 0.001$) (Table 2).

Discussion

Our study suggested the potential clinical benefits of GLP-1RA among patients with co-existing asthma and DM. In the current cohort, patients treated with GLP-1RA had significantly fewer asthma exacerbations of all severities, ranging from those managed in the outpatient setting to those requiring hospitalization. These findings may suggest the potential benefit of using GLP-1RA as an add-on therapy for DM patients with co-existing asthma, with benefits beyond DM and body weight control, but also fewer asthma exacerbations. The findings in this study provided insights into dedicated clinical trials to demonstrate the clinical value of GLP-1RA among patients with co-existing asthma and DM.

The potential benefits of GLP-1RA have been extensively studied in recent years. The benefits range from regulating neuroinflammatory pathways that contribute to asthma pathogenesis,[39] reducing asthma development in diabetic patients,[40] improving asthma control,[41] better lung function[42] and reducing asthma exacerbation risks.[43,44] The benefits may be driven by the effects on mechanistic effects of GLP-1 on pulmonary function and disease. In murine models of lung injury, the administration of exogenous GLP-1RAs has been shown to confer significant protection against pulmonary inflammation and airway hyperresponsiveness.[45] The benefits observed warrants proper assessment by measuring asthma outcomes in different dimensions, such as exacerbation of different severities, and by including a comparator arm.

Our study has an advantage over other published studies regarding the role of GLP-1-based therapies in patients with DM and asthma. First, we chose DPP-4i as the comparator arm instead of other diabetic medications. As both GLP-1RA and DPP-4i work along the same pathway, they are not recommended for concomitant use.[46] When compared with other studies, this strength is more prominent. Kimura et al[28] compared GLP-1RA and DPP-4i with metformin, which is the first-line treatment for DM,[46] while GLP-1RA and DPP-4i were mainly used as an add-on treatment to metformin. Wang et al[24] compared GLP-1RA with sulfonylureas, which are one of the most commonly used antihyperglycemic agents, given their low cost and availability. A head-to-head comparison of GLP-1RA and DPP-4i is ideal, as they are not recommended for concomitant use. Our study also had a prolonged follow-up period to assess the various outcomes. In this study, we demonstrated the potential clinical benefits of GLP-1RA over DPP-4i as an add-on therapy for reducing asthma exacerbations of different severities among patients with asthma and DM. This highlights the importance of personalized therapy among patients with different comorbidities, with the combination of DM and asthma being an example.

In the current study, the number of patients prescribed with GLP-1RA and DPP-4i differs, which can be explained by the differences in indications of the two drugs. In view of this, we performed propensity score matching with optimal full matching implemented. By doing this, we matched the baseline characteristics of the patients prescribed with GLP-1RA and DPP-4i without changing the nominal numbers of subjects in each group. This can handle the issues of possible confounders from the difference in baseline characteristics.

Although DM and asthma are both common medical conditions worldwide, the co-existence of both conditions is also well reported, with different proposed mechanisms linking these two conditions together.[47–49] As such, it is important to consider this combination as a specific condition in which personalized therapy can be offered. The results of this study indicate that a diabetic drug might have potential benefits beyond diabetic care but also in improving asthma control with fewer exacerbations. The possible mechanism could be related to the inhibitory effect on airway inflammation, as demonstrated in animal models.[50] The benefits could also be related to the weight reduction effect of GLP-1RA.[51] These two properties of GLP-1RA could potentially explain the superiority of GLP-1RA over DPP-4i among patients with DM and asthma. As such, among patients with DM and asthma, GLP-1RA could be considered as the add-on diabetic medication of choice.

Our study had several limitations. First, the majority of the patients included in this study were Chinese, which may have affected generalizability. However, we also reported similar findings, as mentioned in studies conducted in other countries. Also, the effect of GLP-1RA is unlikely to be affected by ethnicity. Second, the lung function parameters and symptom burden were not assessed. We assessed asthma severity using the pharmacotherapy they received, that is, GINA Steps, which is a well-recognized way to assess asthma severity. For GINA Steps, it was defined by the asthma medication at the study start. But the treatment and severity of asthma may vary over time, which is another limitation

that we need to acknowledge. While the patients prescribed with GLP-1RA and DPP-4i were matched in the study, potential residual confounding from BMI, diabetes severity, smoking statis and concurrent diabetes medications were possible. Some of these factors might affect asthma exacerbation risks, while some do not. Afterall, the factors that have critical importance were being matched and the impact from the factors not matched may not be a major one. For the outcomes in this study, all exacerbations necessitating the attendance of public hospitals and clinics were captured, while those attending private clinics were not. This may underestimate the number of mild asthma exacerbations, but the impact on more severe ones, such as those requiring hospitalization, is less likely to be affected. Third, only asthma exacerbations, but not asthma control, as measured by changes in the asthma control test score or lung function changes, were measured as the outcomes. However, asthma exacerbation carries a higher burden to patients as well as the healthcare system, and it is also one of the most important criteria to decide on add-on asthma therapy, such as biologics. Lastly, the number of patients treated with GLP-1RA was relatively small as the choices of GLP-1RA were limited at the time of this study. Future prospective studies including clinical trials are valuable to validate the observation.

Conclusion

Among adults with co-existing asthma and diabetes in Hong Kong, GLP-1RA use was associated with fewer asthma exacerbation events compared with DPP-4i use. The potential mechanism can be linked to the anti-inflammatory property of GLP-1RA, while validating the results from a large-scale study involving more subjects is warranted.

Abbreviations

GLP-1, Glucagon-like peptide-1; GLP-1RA, GLP-1 receptor agonists; DPP-4i, Inhibitors of dipeptidyl peptidase-4; DM, Diabetes mellitus; HKHA, Hong Kong Hospital Authority; CDARS, Clinical Data Analysis and Reporting System; PPV, Positive predictive value; ICD-9, International Classification of Diseases, 9th Revision; CCI, Charlson comorbidity index; ICU, Intensive care unit; SD, Standard deviation; IQR, Interquartile range; PSM, Propensity score matching; SMDs, standardized mean difference; ATT, average treatment effect on the treated; BMI, Body mass index; GINA, Global Initiative for Asthma.

Data Sharing Statement

All available data are presented in the manuscript and no additional data are provided.

Ethics Approval and Informed Consent

This study was approved by the Institutional Review Board of the University of Hong Kong and the Hospital Authority Hong Kong West Cluster (UW 23-510). Patient informed consent was waived as this was a retrospective study without active patient recruitment, and all retrieved clinical data were de-identified. This study was conducted in compliance with the principles of the Declaration of Helsinki.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The author reports no conflicts of interest in this work.

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